If you or someone you love has lung cancer, this booklet can help you learn about treatments called targeted therapies. For some subtypes of lung cancer, targeted therapy can be more effective and cause fewer side effects. Targeted therapy drugs “target” specific changes found in some cancers that cause them to grow, divide, and spread. Targeted therapy for lung cancer is most often used on its own, but may be combined with other treatments.

Targeted therapy is not for everyone. Read on to learn more about targeted therapy and the biomarker tests you need to find out if it may be right for you. For information about other kinds of lung cancer treatments, including immunotherapy and chemotherapy, visit www.CancerSupportCommunity.org/Lung.
What is Targeted Therapy?

Targeted therapy is a newer form of cancer treatment. In recent years, scientists have learned more about what makes cancer cells grow out of control. They have found ways that cancer cells are unlike normal cells, and have figured out how to develop drugs that “target” some of these differences.

Targeted therapies block the action of certain genes, proteins, or molecules that cause cancer to grow and spread. Most lung cancer targeted therapies are taken by mouth as a pill.

IS TARGETED THERAPY RIGHT FOR YOU?

Today, targeted therapy is used to treat advanced or metastatic non-small cell lung cancer (NSCLC). So far, no targeted therapy is available for patients with small cell lung cancer (SCLC) outside a clinical trial, but research is ongoing. Your doctor will need to test your tumor for biomarkers to find out if targeted therapy is right for you. This is called biomarker testing. (See page 4 for more info on biomarkers and testing)
HOW TARGETED THERAPY COMPARES

Some of the most common cancer treatments include:

**TARGETED THERAPY**
Targeted therapy targets specific driver mutations that cause cancers to grow, divide, or spread. Doctors test tumors for these mutations (biomarkers) to find out if targeted therapy should work. Diarrhea and skin problems, including rashes, are the most common side effects.

**SURGERY**
Surgery is an operation to remove the cancer (or part of it) from your body. It is not always possible or helpful. When it is thought that the cancer can be completely removed, it is often the first treatment. The most common side effects are pain, fatigue, bleeding, swelling around the surgical site, and infection.

**CHEMOTHERAPY**
Chemotherapy (also called chemo) uses drugs to attack and kill cancer cells. These very strong drugs attack fast-growing cells like cancer. Chemo can cause side effects like hair loss, nausea, mouth sores, and low white blood cell counts.

**RADIATION THERAPY (RADIOTHERAPY)**
Radiation therapy uses strong energy beams, such as very strong x-rays, electrons, or protons, to kill cancer cells and shrink tumors. Radiation can also damage normal tissue or organs, so it is carefully focused to reduce that damage. You may experience redness, burns, or hair loss in the area being treated. Other possible side effects include fatigue, loss of appetite, and nausea.

**IMMUNOTHERAPY**
Immunotherapy works by making the immune system stronger so it can fight cancer better. The immune system helps your body fight infections and other diseases, like cancer. But sometimes cancers learn how to avoid the immune system and grow anyway. Immunotherapy works to turn the immune system back on to fight the cancer. Common side effects include fatigue, skin problems, fever, and shortness of breath. Most side effects are mild, but some can be severe.
What are Biomarkers and Biomarker Testing?

Biomarkers are features of your tumor that can be measured to help guide your therapy. Your biomarker test results help your doctor match targeted therapies to the specific molecular makeup of the cancer you have. This is part of how your doctor decides which treatments will work best for you.

Several biomarkers are important to people with advanced non-small cell lung cancer, and researchers are finding more each year. Page 8 has a list of biomarkers and the targeted therapies that can be used in patients with those biomarkers. Research is ongoing in small cell lung cancer (SCLC) but, so far, there are no approved targeted therapies for SCLC patients available outside a clinical trial.
WHO SHOULD GET BIOMARKER TESTING?
All patients with advanced or recurrent non-small cell lung cancer (NSCLC) should ask their health care team to be tested for biomarkers. As additional targeted therapies become available, biomarker testing may be recommended for early stage NSCLC and small cell lung cancer (SCLC). Today, the main reason to get biomarker testing if you have early-stage NSCLC or SCLC is to see if you can join certain clinical trials. Be sure to ask your doctor whether there might be a clinical trial that is right for you.

WHEN SHOULD YOU BE TESTED?
You should get tested when you are first diagnosed with advanced lung cancer. Biomarker testing should be done before starting treatment. Patients who test positive for certain biomarkers may not respond as well to standard chemotherapy or immunotherapy. For this reason, it can be better to wait a few weeks for the results of all biomarker tests, even if this means delaying start of therapy. Testing may also be useful when your targeted therapy stops working, or when your cancer comes back.

WHERE DO YOU GET TESTED?
When possible, your biopsy (tissue and/or fluid sample) should be collected by a dedicated thoracic doctor at a center that does many such biopsies per week. Blood may also be collected. Then these samples are sent to a lab to run the tests.

Not every hospital has a lab capable of testing for biomarkers. If this is not an option where you are receiving care, ask if your doctor can send your samples out for testing. If you are told that testing is not an option, you should consider getting a second opinion at a cancer center or hospital where these tests can be done. Talking with a second doctor can often help you better understand your cancer and how to treat it. A second opinion can also make you feel more confident that you are making the right choices.

WHAT SHOULD YOU BE TESTED FOR?
If you have advanced NSCLC, ask to have your tumor tested for biomarkers, especially EGFR, ALK, BRAF, ROS1, NTRK, and PD-L1. This may be done using a multi-panel test that looks for all the biomarkers for which there currently are approved targeted therapies. A current list of biomarkers and the currently approved therapies that target those specific cancer subtypes is on page 8. The test also looks for biomarkers for which targeted therapies are being tested in clinical trials. For example, targeted therapies are being studied for NSCLC that tests positive to KRAS, RET and MET, as well as for SCLC.

WHY IS BIOMARKER TESTING IMPORTANT?
Because they are designed to work against a certain target, most targeted therapies are only used when a biomarker test shows that they might be helpful. Patients that test positive for targeted therapy biomarkers may not respond as well to standard chemotherapy. PD-L1, on the other hand, is a biomarker for the use of immunotherapy. If your tumor is negative for the other biomarkers listed above and has high PD-L1, you are likely to have better results with an immunotherapy drug. But patients with biomarkers for targeted therapies should start out with targeted therapy, rather than immunotherapy. This is why it is very important to wait until ALL biomarker testing results have been returned, if possible, before starting treatment. Patients matched with their treatment based on biomarker testing may live a better and longer life.
Getting Targeted Therapy

HOW IS TARGETED THERAPY GIVEN?
Most often, targeted therapy is given in the form of a pill that you take at home once or twice a day. The pill may need to be taken at a certain time of day, with or without food or liquid. You need to remember to take the pill.

A few targeted drugs are given by IV (into a vein), sometimes in combination with chemotherapy. If this is the case, you may have to go into the hospital every 3 to 4 weeks for treatment. Be sure to ask how your treatment works. Let your health care team know of anything that could get in the way of you following the treatment plan.

TARGETED THERAPY FOR LUNG CANCER
Different types of targeted therapy are used to treat lung cancer. Most require a biomarker test, but some do not yet have a good biomarker.

ONLINE PATIENT GROUPS THAT DISCUSS SPECIFIC TARGETS AND THEIR THERAPIES
To connect online with others who test positive for the same biomarkers as you, visit:

- EGFR Resisters [www.egfrcancer.org](http://www.egfrcancer.org)
- ALK Positive [www.alkpositive.org](http://www.alkpositive.org)
- ROS1ders [www.ros1cancer.com](http://www.ros1cancer.com)
- Exon 20 Group [www.exon20group.org](http://www.exon20group.org)
Therapies that target the tumor’s blood vessel growth (angiogenesis), known as VEGF inhibitors, currently do not yet have a good biomarker test and are most often given along with another treatment. See the charts for more information about VEGF inhibitors.

The key biomarkers that play a role in lung cancer — and for which there are matching FDA-approved treatments — are EGFR, ALK, BRAF, ROS1, NTRK, and PD-L1. The chart on page 8 lists biomarkers, which drugs are approved to target them, and what percent of people with lung cancer have this biomarker. KRAS, the most common lung cancer biomarker, currently does not have a matching approved targeted therapy.

Researchers have also found other biomarkers that may be relevant to lung cancer. They include HER2, MET, MEK1, and RET. Drugs have not yet been approved to target them, but might be available through clinical trials.

Ask your doctor:

- If your tumor has been tested for these biomarkers.
- About targeted therapy options when you are diagnosed. Ask again in the future, in the likely case that more options become available.
- About the possibility of receiving treatment through a clinical trial.

New biomarkers continue to be discovered, and new drugs are being found that work against them.

**RECEIVING TARGETED THERAPY THROUGH A CLINICAL TRIAL**

Many patients with lung cancer decide to receive their treatment through a clinical trial.

Clinical trials are research studies to test new treatments or learn how to use existing treatments better. Every drug must be tested in clinical trials before it can be used with patients. Ask your doctor if a clinical trial might be right for you — before you start treatment or when you are looking at new treatment options.

**KEY THINGS TO KNOW:**

- People who receive their treatment through a clinical trial receive high quality care.
- There are rules about who can join each trial, so they are not available for every patient.
- Not all treatment centers offer clinical trials. And not all centers offer the same clinical trials.
- There are laws and review boards to protect the safety of people who participate.
- No one receives a placebo or “sugar pill” in place of appropriate treatment. You will always receive treatment that is at least “standard of care.”
- If you join a clinical trial, you can leave at any time and for any reason.
- Often, the trial pays the costs of the drug being studied. Then, your health insurance and your copay cover “standard” treatment costs. Be sure to ask what costs you may incur.
- If you get your treatment through a clinical trial, you may need to visit your treatment center more often.
New treatments become available all the time so this may not be a complete list. **These are the latest targeted therapies that are available as of August 2019.** For the latest information go to www.CancerSupportCommunity.org/Lung.

<table>
<thead>
<tr>
<th>BIOMARKER</th>
<th>% OF NSCLC WITH THIS BIOMARKER</th>
<th>DRUG NOTES (+ MEANS A POSITIVE TEST)</th>
</tr>
</thead>
</table>
| **EGFR**  | 15%                            | • For EGFR+ metastatic NSCLC  
- Depending on the exact EGFR mutation, can be used as 1st treatment: Gilotrif, Iressa, Tagrisso, Tarceva, and Vizimpro  
- Can be used when other EGFR drugs have stopped working: Tagrisso  
- All given as a once-daily pill  
• For advanced squamous cell NSCLC: Portrazza  
- Given by vein in combination with chemotherapy |
|           |                               | **Drug generic (and brand) names** |
|           |                               | afatinib (Gilotrif®)  
daacomitinib (Vizimpro®)  
erlotinib (Tarceva®)  
gefitinib (Iressa®)  
nectitumumab (Portrazza®)  
osimertinib (Tagrisso®) |
| **ALK**   | 5%                             | • For ALK+ metastatic NSCLC  
- Alecensa and Xalkori are given as a twice-daily pill  
- Alunbrig, Lorbrema, and Zykadia are given as a once-daily pill |
|           |                               | **Drug generic (and brand) names** |
|           |                               | alectinib (Alecensa®)  
brigatinib (Alunbrig®)  
ceritinib (Zykadia®)  
crizotinib (Xalkori®)  
lorraineib (Lorbrena®) |
| **BRAF**  | 2-4%                           | • For BRAF+ NSCLC  
- Tafinlar is given as a twice-daily pill  
- Mekinist is given as a once-daily pill  
- Given in combination with each other |
|           |                               | **Drug generic (and brand) names** |
|           |                               | dabrafenib (Tafinlar®)  
trametinib (Mekinist®) |
| **ROS-1** | 1-2%                           | • For ROS1+ metastatic NSCLC  
- Xalkori is given as a twice-daily pill  
- Rozlytrek is given as a once-daily pill |
|           |                               | **Drug generic (and brand) names** |
|           |                               | crizotinib (Xalkori®)  
extrectinib (Rozlytrek™) |
| **NTRK**  | 0.2-0.3%                       | • For NTRK+ metastatic solid tumors, including NSCLC  
- Rozlytrek is given as a once-daily pill  
- Vitrakvi is given as a twice-daily pill |
|           |                               | **Drug generic (and brand) names** |
|           |                               | extrectinib (Rozlytrek™)  
larotrectinib (Vitrakvi®) |
| **VEGF**  | No biomarker required for treatment | • For non-squamous advanced NSCLC: Avastin  
- As second treatment for metastatic NSCLC: Cyramza  
- Given by IV (in the vein) every 3 weeks, often in combination with chemo |
|           |                               | **Drug generic (and brand) names** |
|           |                               | bevacizumab (Avastin®)  
- and its biosimilars like bevacizumab-awwb (Mvasi®)  
ramucirumab (Cyramza®) |
Targeted therapies treat the cancer cells with less harm to normal cells. Not all people get all side effects. Be sure to tell your health care team about the side effects you have.

New treatments become available all the time so this may not be a complete list. These are the latest targeted therapies that are available as of August 2019. For the latest information go to www.CancerSupportCommunity.org/Lung.

<table>
<thead>
<tr>
<th>TYPE OF THERAPY</th>
<th>COMMON SIDE EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EGFR INHIBITORS</strong></td>
<td>• Skin changes (acne-like rash, dry skin, itchiness)</td>
</tr>
<tr>
<td>• afatinib (Gilotrif®)</td>
<td></td>
</tr>
<tr>
<td>• dacomitinib (Vizimpro®)</td>
<td></td>
</tr>
<tr>
<td>• erlotinib (Tarceva®)</td>
<td></td>
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<tr>
<td>• gefitinib (Iressa®)</td>
<td></td>
</tr>
<tr>
<td>• necitumumab (Portrazza®)</td>
<td></td>
</tr>
<tr>
<td>• osimertinib (Tagrisso®)</td>
<td></td>
</tr>
<tr>
<td><strong>ALK INHIBITORS</strong></td>
<td>• Changes in vision (blurry vision)</td>
</tr>
<tr>
<td>• alectinib (Alecensa®)</td>
<td></td>
</tr>
<tr>
<td>• brigatinib (Alunbrig®)</td>
<td></td>
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<tr>
<td>• ceritinib (Zykadia®)</td>
<td></td>
</tr>
<tr>
<td>• crizotinib (Xalkori®)</td>
<td></td>
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<tr>
<td>• lorlatinib (Lorbrena®)</td>
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<tr>
<td><strong>BRAF INHIBITORS</strong></td>
<td>• Fever</td>
</tr>
<tr>
<td>• dabrafenib (Tafinlar®)</td>
<td></td>
</tr>
<tr>
<td>• trametinib (Mekinist®)</td>
<td></td>
</tr>
<tr>
<td>• Changes to skin (thickening, rash, warts, dryness)</td>
<td></td>
</tr>
<tr>
<td>• Fatigue</td>
<td></td>
</tr>
<tr>
<td>• Nausea and vomiting</td>
<td></td>
</tr>
<tr>
<td>• Sensitivity to the sun</td>
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</tr>
</tbody>
</table>
## SIDE EFFECTS BY TYPE OF DRUG

### ROS1 INHIBITORS
- **crizotinib (Xalkori®)**
- **entrectinib (Rozlytrek™)**

- Changes in vision (blurry vision)
- Diarrhea
- Nausea and vomiting
- Constipation
- Fatigue
- Loss of appetite or change in taste
- Swelling

With Rozlytrek only:
- Dizziness
- Abnormal touch sensation
- Shortness of breath

**Rare but serious side effects may include:**
- Problems to the heart, liver, kidneys, eyes, central nervous system (Rozlytrek only), or lungs (Xalkori only)

### NTRK INHIBITORS
- **entrectinib (Rozlytrek™)**
- **larotrectinib (Vitrakvi®)**

- Fatigue
- Nausea and vomiting
- Constipation or diarrhea
- Dizziness
- Anemia (Vitrakvi only)

Regular blood tests are needed to check liver function.

With Rozlytrek only:
- Swelling
- Change in taste
- Abnormal touch sensation
- Shortness of breath

**Rare but serious side effects may include:**
- Problems to the liver or nervous system, and for Rozlytrek with the heart, kidneys, and eyes

Let your doctor know if you have dizziness, unclear speech, problems walking, or are feeling tingling, burning or numbness. (Most often occurs in the first 3 months.)

### VEGF or ANGIOGENESIS INHIBITORS
- **bevacizumab (Avastin®)** and its biosimilars like bevacizumab-awwb (Mvasi®)
- **ramucirumab (Cyramza®)**

- High blood pressure
- Changes to skin (dryness, rash)
- Diarrhea
- Nosebleeds
- Loss of appetite
- Low blood counts
- Weakness
- Upper respiratory infection
- Runny nose

**Rare but serious side effects may include:**
- Stroke
- Heart attack
- Blood clots
- Wounds that may not heal
- Tears in the stomach or bowel wall
MANAGING SIDE EFFECTS OF TARGETED THERAPY
Targeted therapies often have milder side effects than other cancer treatments. Skin rash is common but doesn’t occur at all in some people. Ask about it before you start treatment so that you can have medicine for it available if needed. Rashes often get better with time. As with any cancer drug, remember these steps:

Before you start treatment: Ask about the side effects of any drug you consider. Ask what you might experience, and how you can manage it. There may be medicine you can take or use to prevent or ease symptoms.

During/after treatment: Report any side effects you experience. Tell your health care team about any change you notice, however small. Some side effects can get worse quickly if they are not treated.

QUESTIONS TO ASK YOUR HEALTH CARE TEAM

- What type of lung cancer do I have?
- If it is advanced non-small cell lung cancer, has my tumor biopsy been sent for biomarker testing for EGFR, ALK, BRAF, ROS1, NTRK, and PD-L1?
- If so, what do the results mean for me?
- Is targeted therapy available for my lung cancer type? If so, what kind?
- Are there any clinical trials for targeted therapy that might be right for me? How do I find out more about them?

For each treatment that is recommended:
- What is the goal of this treatment? What are the risks?
- Is this treatment available in pill form? If yes, how often will I need to take pills? Do I take the pills with or without food?
- If this treatment is given by IV, where will I go to receive treatment and how long will each session take? Will I need someone to drive me home after treatment?
- Can/should I eat or drink before or after treatment? Is there any food or drink I should avoid while on this treatment?
- What side effects should I expect (short- and long-term)?
- What can I do to prepare for this treatment?
- How long will I need to be on this treatment?
- How will we know if this treatment is working?
- If it stops working, what is the next treatment option?
- How much will this treatment cost?
- Will I need other cancer treatments at the same time?
- How will this treatment affect my daily routine? Will I be able to do my usual daily activities?
- Whom should I call if I have questions or problems:
  During office hours? Name: ___________________ Phone Number: _______________
  After hours and weekends? Name: __________________ Phone Number: _______________
Lung Cancer Information, Survivorship & Support

Cancer Support Community • 888-793-9355 • www.CancerSupportCommunity.org
American Cancer Society • 800-227-2345 • www.cancer.org
CancerCare • 800-813-4673 • www.cancercare.org
Cancer.net • 888-651-3038 • www.cancer.net
GO2 Foundation for Lung Cancer • 800-298-2436 • www.go2foundation.org
LUNGevity Foundation • 321-407-6100 • www.LUNGevity.org
National Cancer Institute (NCI) • 800-422-6237 • www.cancer.gov
NCI Clinical Trial Information • 800-422-6237 • www.cancer.gov/ClinicalTrials
Patient Advocate Foundation • 800-532-5274 • www.patientadvocate.org

Cancer Support Community Resources

Cancer Support Helpline® — Have questions, concerns or looking for resources? Call CSC’s toll-free Cancer Support Helpline (888-793-9355), available in 200 languages Mon - Fri 9am - 9pm ET.

Open to Options® — Need help making a cancer treatment decision? Our trained specialists can help you create a list of questions to share with your doctor. Make an appointment by calling 888-793-9355 or by contacting your local CSC or Gilda’s Club.

Frankly Speaking About Cancer® — Trusted information for cancer patients and their loved ones is available through publications, online, and in-person programs.

Services at Local CSCs and Gilda’s Clubs — With the help of 170 locations, CSC and Gilda’s Club affiliates provide services free of charge to people touched by cancer. Attend support groups, educational sessions, wellness programs, and more at a location near you. www.CancerSupportCommunity.org/FindLocation.

Cancer Experience Registry® — Help others by sharing your cancer patient or cancer caregiver experience via survey at www.CancerExperienceRegistry.org.

MyLifeLine — CSC’s private, online community allows patients and caregivers to easily connect with friends and family to receive social, emotional, and practical support throughout the cancer journey and beyond. Sign up at www.MyLifeLine.org.

Grassroots Network — Make sure your voice is heard by federal and state policy makers on issues affecting cancer patients and survivors by joining our Network at www.CancerSupportCommunity.org/become-advocate.

FRANKLY SPEAKING ABOUT CANCER: LUNG CANCER PROGRAM PARTNERS:

THIS PROGRAM WAS MADE POSSIBLE THROUGH GENEROUS SUPPORT FROM:

The Cancer Support Community and its partners provide this information as a service. This publication is not intended to take the place of medical care or the advice of your doctor. We strongly suggest consulting your doctor or other health care professionals to answer questions and learn more.

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